Huntington's Disease Team

Grant Award Details

Huntington's Disease Team

Grant Type: Disease Team Planning

Grant Number: DT1-00700

Investigator:

Name:	Leslie Thompson
Institution:	University of California, Irvine
Type:	PI

Disease Focus: Huntington's Disease, Neurological Disorders

Award Value: $41,953

Status: Closed

Grant Application Details

Application Title: Huntington's Disease Team

Public Abstract:

Huntington's disease (HD) is a devastating degenerative brain disease with a 1 in 10,000 risk of having a mutation that inevitably leads to death. These numbers do not fully reflect the large societal and familial cost of HD, which requires extensive caregiving. HD has no effective treatment or cure and symptoms progress without stopping for 15-20 years, with onset typically striking in midlife. Because HD is genetically dominant, the disease has a 50% chance of being inherited by the children of patients. Symptoms of the disease include uncontrolled movements, difficulties in carrying out daily tasks or continuing employment, and severe psychiatric manifestations including depression. Specific regions of the brain are severely affected, most notably the striatum. Current treatments only treat some symptoms and do not change the course of the disease, therefore a completely unmet medical need exists. Human embryonic stem cells (hESCs) offer a possible long-term treatment that could relieve the tremendous suffering experienced by patients and their families. HD is the 3rd most prevalent neurodegenerative disease, but because it is entirely genetic and the mutation known, a diagnosis can be made with certainty and clinical applications of hESCs may provide insights into treating brain diseases that are not caused by a single, known mutation. Trials in mice where protective factors were directly delivered to the brains of HD mice have been effective, suggesting that delivery of these factors by hESCs may help patients. In addition, transplantation of fetal brain tissue in HD patients suggests that replacing neurons that are lost may also be effective. While encouraging, the ability to differentiate hESCs into neuronal populations offers a powerful and sustainable alternative for cell replacement. Further, hESCs offer an opportunity to create cell models in which to identify earlier markers of disease onset and progression and for drug development.

A core group of HD and stem cell experts together with clinicians experienced in stem cell and HD clinical trials have been assembled by the PI to initiate the planning process for a hESC-based therapeutic trial for HD within four years. While feasible, in order for the potential of hESCs in HD to be realized, a very forward thinking disease team effort will allow the most experienced investigators in HD, stem cell research and clinical trials to come together and determine the best way to treat the disease. This planning grant would allow for these interactions to occur in a structured and consistent manner. The planning award will be used to identify critical gaps in our knowledge, available technology, and areas of expertise that need to be addressed prior to moving hESC-based therapy for HD into the clinic. Because the work proposed would entail the use of non-NIH approved hES cell lines, it would be ineligible for Federal funding.

Statement of Benefit to California:	The disability and loss of earning power and personal freedom resulting from Huntington's disease (HD) is devastating and creates a financial burden for California. Individuals are struck in the prime of life, at a point when they are their most productive and have their highest earning potential. Further, as the disease progressives, individuals require institutional care facilities at great financial cost. Therapies using human embryonic stem cells (hESCs) have the potential to change the lives of hundreds of individuals and their families, which brings the human cost into the thousands. Further, hESCs from HD patients will help us understand the factors that dictate the course of the disease and provide a resource for drug development. For the potential of hESCs in HD to be realized, a very forward thinking disease team effort will allow the most experienced investigators in HD and stem cell research and clinical trials to come together and determine the best way to treat the disease. This planning grant would allow for these interactions to occur in a structured and consistent manner. California researchers need the resources needed to allow researchers having the necessary expertise and technologies to come together as a team to develop hESCs into viable treatments. The federal constraints on hESCs create a critical need for the development of treatments using hESCs supported and staffed with non-federal funds. We have assembled a strong core team of California-based senior investigators to plan goals and strategies for taking hESCs from the lab to the clinic. The planning award will be used to identify critical gaps in our knowledge, available technology, and areas of expertise that need to be addressed prior to moving SC-based therapy for HD into the clinic. We will also put in place critical milestones to be met and to formalize a management plan that will ensure that the milestones are achieved. We will build on existing regional stem cell resources used by scientists from California institutions. Anticipated benefits to the citizens of California include: 1) development of new cell-based treatments for Huntington's disease with application to other neurodegenerative diseases such as Alzheimer's and Parkinson's diseases that affect thousands of individuals in California; 2) improved methods for following the course of the disease in order to treat HD as early as possible before symptoms are manifest; 3) development of intellectual property that could form the basis of new biotech startup companies; and 4) improved methods for drug development that could directly benefit citizens of the state. With the proposed disease team our vision of bringing treatments for HD and other neurodegenerative diseases to the clinic can become a reality.

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